

ural history model to project clinical and/or economic outcomes. **METHODS:** The subset of stage I-III colon cancer patients who will experience recurrence face a constant rate  $\rho_d$  of transition from undetectable to theoretically detectable recurrence during a given interval. These same patients face a constant rate  $\rho_u$  of transition from resectable (i.e. potentially curable) to unresectable metastatic disease with a minimum interval  $\Delta t$  between the point of detectability and the point of unresectability. A third constant rate parameter  $\rho_s$  will determine when, on average, individuals develop recurrence-related symptoms prompting them to seek medical advice before the next scheduled evaluation. The mean point of symptom development will follow the point at which a recurrence becomes detectable by a span of at least  $\Delta t$ . However, a normally distributed error term  $\epsilon_d$  will mean that, for a given simulated patient, symptoms may initiate before or after the patient reaches unresectability. **RESULTS:** A best-fitting set of these natural history parameters can be selected by calibrating to targets of time-to-detection of recurrence, time-to-death, and proportion of patients who present with recurrence-related symptoms prior to scheduled assessments. **CONCLUSIONS:** The data sources for these targets can be existing experimental, observational, or registry data where follow-up schedule and compliance levels are known.

## PRM56

## DIFFERENTIAL DISCOUNTING: QUESTIONING THE ASSUMPTION OF HEALTHCARE RESOURCE FUNGIBILITY OVER TIME

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**OBJECTIVES:** Recent work on differential discounting of cost and health effects has reached a degree of consensus in a previously strongly divided debate. Put simply, it holds that the discount rate applied to health effects should equal the discount rate for costs, less the growth rate of either the cost-effectiveness threshold or the consumption value of health, depending on the objectives of the health system. Assuming positive growth in the threshold or the value of health, this implies the cost-effectiveness of preventative interventions improves relative to the situation under equal discounting. **METHODS:** We show how recent analyses of differential discounting implicitly assume healthcare funds to be completely fungible over time. This assumption is difficult to justify in the context of publically funded healthcare systems that exhaust budgets annually. Assuming funds are not fungible results in alternative differential discount rates: in this case, the discount rate on costs should be adjusted upwards by either the growth rate of the threshold or the consumption value of health. **RESULTS:** Under these discount rates, interventions that impose costs in future periods become more cost-effective relative to the situation under equal discounting, rather than those which yield health gains in the future. Indeed, the cost-effectiveness of preventative interventions that reduce future healthcare costs will deteriorate under such alternative differential discounting. Consequently, interventions' cost-effectiveness may differ greatly between the two differential discounting schemes. **CONCLUSION:** Cost-effectiveness estimates can be highly sensitive to discounting; therefore the theory underpinning discount rates needs to be robust. This analysis shows that the current understanding of differential discounting needs to be re-examined. CEA authorities in countries currently employing differential discounting such as Belgium and The Netherlands and those contemplating it such as England and Wales should consider these issues carefully.

## PRM57

## REVISITING HPV VACCINATION: WHY EXISTING CEAS UNDERESTIMATE THE VACCINE'S COST-EFFECTIVENESS AND INCORRECTLY ESTIMATE ITS THRESHOLD PRICE

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**OBJECTIVES:** Existing cost-effectiveness analyses (CEAs) of Human Papillomavirus (HPV) vaccination assume cervical screening remains unchanged. However, current screening intensities are unlikely to be cost-effective due to the likely reduction in disease incidence in vaccinated women. Therefore, reductions in screening intensity are probable. The cost-effectiveness attributable to vaccination varies with screening intensity. The assumption of unaltered screening leads to an underestimation of vaccine cost-effectiveness relative to when screening intensity is reduced. Furthermore, failure to consider other screening intensities yields an incomplete efficient frontier in the cost-effectiveness plane. This can lead to an incorrect estimate of the price at which vaccination becomes marginally cost-effective for a given cost-effectiveness threshold. **METHODS:** We review cost-effectiveness estimates for a wide range of screening only and vaccination plus screening strategies from a model used to estimate vaccine cost-effectiveness in the The Netherlands. We indicate what comparison was used to estimate vaccine cost-effectiveness in previous studies, show what comparisons would be more appropriate and explain how these differ. **RESULTS:** We then show why the cost-effectiveness of adding vaccination to a given screening strategy is not the appropriate basis to determine if the vaccine is cost-effective or the threshold price. Rather, both should be determined by the ICER between the most costly efficient screening only strategy and the least costly vaccination plus screening strategy, even where this least costly vaccination plus screening strategy is not the optimal strategy for a given threshold. **CONCLUSIONS:** CEAs of HPV vaccination may no longer be policy or research priorities following widespread reimbursement and precipitous price reductions. However, the methodological issues raised here are pertinent to both any future CEA of an enhanced vaccine with protection against more HPV types and more generally to cases in which the cost-effectiveness of complementary interventions are not independent.

## PRM58

## METHODODOLOGICAL REVIEWS OF ECONOMIC EVALUATIONS IN HEALTH CARE: ARE THEY USEFUL?

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**INTRODUCTION AND OBJECTIVES:** The increasing amount of economic evaluations in health technologies published during the last decades have generated the concern about their methodological features. The aim of this study is, firstly, to explore methodological reviews and to detect their main research topics and, secondly, to appraise their usefulness for economic evaluation practice. **METHODS:** We performed systematic searches in electronic databases (Scopus, Medline and Pubmed) of methodological reviews published in English, period 1990-2010. We selected those articles whose main purpose was to review and assess the applied methodology. Then we classified data according to study objectives, period of the review, number of reviewed studies, methodological items assessed and their main conclusions. Additionally, we checked how generalizability issues were considered in the reviews. **RESULTS:** A total of 58 methodological reviews were identified, 42 were published during the period 1990-2001 and 16 during 2002-10. Items most frequently assessed (by 70% of the reviews) were: perspective, uncertainty and discounting. The type of intervention and disease, funding sources, country in which the evaluation took place, type of journal and author's characteristics were also described in the literature. Generalizability issues were only checked in 14 studies, mainly by those published after 2000. **CONCLUSIONS:** there is an increasing activity of reviewing economic evaluation studies aiming to analyse the application of methodological principles and to offer summaries of papers classified by either diseases or health technologies. These reviews are useful to detect literature trends, targets of the studies and possible deficiencies in the implementation of the methods to specific health interventions.

## PRM59

## ESTIMATING THE CONFIDENCE INTERVAL FOR THE COST-EFFECTIVENESS RATIO FROM A FAMILY OF REGRESSIONS ON NET MONETARY BENEFIT

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**OBJECTIVES:** To demonstrate a novel way of deriving the incremental cost-effectiveness ratio (ICER) and associated 95% confidence interval (CI) from the cost-effectiveness acceptability curve (CEAC) generated from a family of regressions on net monetary benefit (NMB). **METHODS:** Definitions and mathematical properties of the ICER, NMB, and CEAC are explored to construct a technique for deriving 95% CIs around the ICER estimated from the CEAC. **RESULTS:** CEA uses the ICER, a measure with statistical issues that preclude easy derivation of confidence intervals. NMB is defined for any willingness-to-pay (WTP) value as:  $NMB = (effectiveness \times WTP) - cost$ . Because NMB is statistically well-behaved, regression analysis can estimate incremental net monetary benefit (INMB) as the parameter estimate associated with treatment.  $INMB = (\text{delta effectiveness} \times WTP) - \text{delta cost}$ . The CEAC is generated from a family of these regressions where the unique members of the family are identified by unique levels of WTP used to calculate NMB. The ICER is the point on the CEAC where the probability of being cost-effective is 50%, because at that point INMB is zero and WTP equals delta cost/delta effectiveness; i.e., the ICER. That point on the CEAC can be identified numerically by simultaneously solving the two equations for INMB from the two regressions that flank estimated INMB of zero. Knowing estimated INMB and the WTP we have two equations and two unknowns, and we solve for delta effectiveness and delta cost. We use a similar procedure on the 95% confidence intervals for two estimated INMBs to find the 95% CI for the ICER. **CONCLUSIONS:** In the case where we estimate the ICER from a family of regressions on NMB to construct the CEAC we can also find the 95% CI of the ICER.

## PRM60

## ASSESSING RELATIVE CLINICAL VALUE ACROSS TUMOR TYPES IN METASTATIC DISEASE

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**OBJECTIVES:** In the absence of increasing budgets, new therapies and resource constraints have necessitated value trade-offs across tumor types and products. Traditional metrics such as median overall survival (OS) may not fully demonstrate the value of individual products in these comparisons. To highlight this, we assessed the value of different innovative cancer drugs relative to their clinical trial comparator using a variety of OS metrics. **METHODS:** We selected novel oncology products used in the treatment of metastatic disease with documented overall survival benefit over comparator at the time of launch. The selected products were: bevacizumab (colorectal cancer, non squamous non-small cell lung cancer), sunitinib (renal cell carcinoma), sorafenib (hepatocellular carcinoma), lenalidomide (multiple myeloma), ipilimumab (melanoma), trastuzumab (breast cancer). Key survival metrics including median OS, mean OS, and landmark survival rates from each analogue's pivotal trials were used to assess the relative value of each analogue. **RESULTS:** The relative value for each analogue differs depending on the survival metric used, suggesting that median OS does not fully capture the value of oncology agents. For example, lenalidomide's relative value is the highest in terms of median OS improvement; however its relative value is diminished when looking at mean OS. Ipilimumab, conversely, shows the highest value in terms of mean OS (attributing benefit to a proportion of patients achieving prolonged survival benefit). Furthermore, sorafenib (HCC) and ipilimumab (melanoma) demonstrate the highest relative value when evaluating 1 year survival improvement.